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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/800,240	PREVELIGE,, PETER E.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 7-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 7-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 30 December, 2003. Claims 4, 7, 9, and 10 were amended, claims 5 and 6 canceled without prejudice or disclaimer, and new claims 13-18 submitted. Claims 1-4 and 7-18 are pending in the instant application.

35 U.S.C. § 112, Second Paragraph

Claims 1-4 and 7-12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

The reference to "triggering assembly" of a viral structural protein in step (ii) is vague and indefinite. It is not readily manifest what this step actually entails? How is "assembly" being activated? What factors, reagents, compounds, and steps are required to activate this step? The reference to "monitoring viral assembly" in step (iv) is also vague and indefinite. It is not readily manifest what biochemical or virological process is being measured (i.e., virus-like particle formation, conical capsid formation, tubular capsid formation, immature particle formation, capsid aggregation, etc.). Applicant needs to clearly and unambiguously set forth the salient structural characteristics of the claimed invention. Perusal of the disclosure reveals an HIV-1 *in vitro* capsid assembly system wherein immature HIV-1 capsids (e.g., conical or spherical) were induced by the addition of salt (e.g., a final concentration of 1 M NaCl) to a purified preparation of the CA protein. Applicant should amend the claim language as supported by the disclosure.

Claims 13-18 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims fail to set forth the salient characteristics of the claimed invention. For instance, claim 13 simply recites "A method comprising the steps of" without setting forth the purpose of said method (i.e., A method for the identification of compounds capable of modulating HIV-1 virion assembly and morphogenesis comprising ...). The reference to "assembling said viral structural protein" in step (ii) is also vague and indefinite. It is not readily manifest what type of biochemical or virological process is encompassed by this step (i.e., virus-like particle formation, conical capsid formation, tubular capsid formation, immature particle formation, capsid aggregation, etc.). Appropriate correction is required. Applicant is directed to the preceding paragraph for suggestions in drafting appropriate claim language.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 7-18 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *University of Rochester*, 358 F.3d 916, 69 U.S.P.Q.2d 1886 (C.A.F.C.

2004).

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for the broadly claimed genus of any **"viral structural protein"**. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). The court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a

genus because it would not reasonably lead those skilled in the art to any particular species.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a nucleotide or amino acid sequence, chemical structure, binding affinity, binding specificity, and molecular weight. The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

The claims of the instant application are directed toward a

poorly defined biochemical method that employs any "**viral structural protein in soluble form**" that is capable of assembling. As set forth *supra*, the disclosure describes an **HIV-1** *in vitro* **capsid (CA)** assembly system wherein immature HIV-1 capsids (e.g., conical or spherical) were induced by the addition of salt (e.g., a final concentration of 1 M NaCl) to a purified preparation of the CA protein. The disclosure does **not** describe the isolation and purification of any other viral structural proteins. The disclosure does not describe an *in vitro* assembly system employing any other viral structural proteins. The only viral structural protein described in the specification is the HIV-1 CA protein. Considering the genotypic/phenotypic heterogeneity of the viruses encompassed by the claim language, the difficulties associated with protein purification (see next rejection below), and the difficulties associated with preparing *in vitro* assembly systems using purified viral components, the skilled artisan would reasonably expect to see additional guidance on these factors in the disclosure. However, the disclosure is clearly directed toward one virus (HIV-1) and one structural protein (CA). Detailed descriptions of other *in vitro* assembly systems employing other viral structura proteins are not provided. Thus, the skilled artisan would reasonably conclude that applicants were in possession of an *in vitro* HIV-1 capsid (CA) assembly system wherein immature HIV-1 capsid formation was induced by the addition of high concentrations of salt.

Applicant is reminded that the written description requirement of a patent specification provides a teaching function, as a *quid pro quo,* in which the public is given meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time. Moreover, while it is true that claimed subject matter of a patent need not be described *in haec verba* in the specification to satisfy the written description requirement,

e.g., *In re Smith*, 481 F.2d 910, 914 [178 USPQ 620] (CCPA 1973), it is also true that the requirement must still be met in some way so as to describe the claimed invention so that one skilled in the art can recognize what is claimed. The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of what a material does, rather than of what it is, usually does not suffice. Finally, as the Supreme Court has cautioned, "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." *Brenner* v. *Manson*, 383 U.S. 519, 536 [148 U.S.P.Q. 689] (1966). Here the applicant has done no more than prepare an *in vitro* HIV-1 CA assembly system employing increasing concentrations of salt to induce immature capsid assembly. The disclosure does not detail the isolation and purification of any other structural protein. The disclosure does not describe the conditions required to induce assembly of said proteins. The term "viral structural protein" encompasses an extremely large genus of genotypically/phenotypically distinct compounds. These proteins display little genetic relatedness and require different purification schemes. Moreover, previous studies have suggested that they also display different requirements for virion assembly (see next rejection). Thus, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed invention at the time of filing.

Claims 1-4 and 7-18 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. As set forth *supra*, the disclosure describes an HIV-1 *in vitro* capsid assembly system wherein immature HIV-1 capsids (e.g., conical or spherical) were

induced by the addition of salt (e.g., a final concentration of 1 M NaCl) to a purified preparation of the CA protein. Appropriately drafted claim language directed toward this embodiment, as supported by the disclosure, would be acceptable. However, the claims are not enabled for the full breadth of coverage directed toward any "viral structural protein in a soluble form".

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

Excessive Claim Breadth

The claims are broadly directed toward any "viral structural protein in a soluble form" that is capable of assembling, presumably into a virus-like particle. This recitation encompasses a large number of structural proteins from a number of genotypically/phenotypically unrelated viruses (Murphy, 1996; Harrison *et al.*, 1996). For instance, the claims encompass viral structural proteins obtained from various members of the following viral familes: *Picornaviridae, Calciviradae, Astroviridae, Togaviridae, Flaviviridae, Coronaviridae, Paramyxoviridae, Rhabdoviridae, Filoviridae, Orthomyxoviridae, Bunyaviridae,*

Arenaviridae, *Reoviridae*, *Birnaviridae*, *Retroviridae*, *Hapadnaviridae*, *Circoviridae*, *Parvoviridae*, *Papovaviridae*, *Adenoviradae*, *Herpesviridae*, and the *Poxviridae*. These viruses all display different virion and physicochemical properties (e.g., morphology, virion size, virion shape, capsid symmetry, capsid structure, presence/absence of peplomers, presence/absence of an envelope, virion molecular mass, pH stability, thermal stability, cation stability, solvent stability, detergent stability). All of these various properties will influence attempts to generate an *in vitro* capsid assembly system. However, with the exception of the HIV-1 CA assembly system described, the disclosure fails to address any of these properties. Moreover, many viruses within the same families often display remarkably different structures and properties. For instance, the *Retroviridae* display four different types of budding particles (e.g., Type A/B, C, D, or lentiviral particles) each involving their own distinct mechanisms, viral proteins, host cofactors, and nucleic acids. Thus, the disclosure would need to provide considerable more guidance to enable the breadth of the claimed invention.

State-of-the-Art

The state-of-the-art as it pertains to understanding virion assembly and morphogenesis is quite complicated. Many viruses display different mechanisms of virion assembly and morphogenesis, even within the same viral families (Harrison *et al.*, 1996). The structural principles governing particle assembly and maturation remain to be elucidated for several viruses (Gross *et al.*, 2000). Those intermolecular interactions governing the process in many cases remain unknown. Thus, the skilled artisan cannot directly extrapolate the findings of the specification to all other viral assembly methods. Painstaking research will be required to ascertain which viral structural proteins, host factors, lipids, and nucleic acids are required for the assembly process of many of

the viruses encompassed by the claim language.

Unpredictability of the Art

Protein purification is an empirical process often requiring extensive trial and error to arrive at a suitable scheme (Coligan *et al.*, 2003). Because of the different structural and physical characteristics of any given protein, particularly unrelated viral structural proteins, different protocols will be required to purify the protein of interest in an active form. A purification procedure that was useful for one viral protein (i.e., HIV-1 CA) will probably not be useful for a different structurally unrelated viral protein. The disclosure fails to provide any guidance pertaining to suitable purification schemes for other viral structural proteins that are encompassed by the claim language.

The generation of *in vitro* virion assembly systems is a complicated process. Generic reaction conditions cannot be applied to all viral systems. For instance, it has been well-documented that different viruses have different assembly requirements. Zdenek *et al.* (2004) note that the Mason-Pfizer monkey virus (MPMV) Gag protein "contains a p12 protein that has no corresponding analogues in most other retroviruses". Furthermore, Gross *et al.* (2000) reported that slightly alkaline to neutral pH was required for efficient HIV-1 virion assembly whereas Rous sarcoma virus-derived proteins required a slightly acidic pH. There is also considerable variation in reaction conditions within the same viral family and even within the same virus. For instance, Gross *et al.* (1997) reported that different assembly protocols were required for CA or CA-NC-RNA assembly reactions. The former reaction required high salt whereas the latter reaction was more efficient at low salt concentrations. Thus, there is considerable variability in the required reaction conditions from virus-to-virus, as well as, assembly proteins derived from the same virus. Thus, the skilled artisan cannot reasonably predict what type of reaction conditions

will suffice for any given structural protein.

Inadequate Direction/Guidance Provided

As set forth *supra*, the claims encompass a large genus of viral structural proteins. Many of these viruses are genotypically/phenotypically unrelated. This is not surprising considering they have all evolved to infect different hosts and tissues. The disclosure fails to provide adequate guidance pertaining to appropriate purification schemes for other viral structural proteins and appropriate *in vitro* virion assembly reaction conditions (i.e., buffer concentrations, salt concentrations, pH, cofactor requirements, nucleic acid requirements, lipid requirements, etc.).

Limited Number of Working Embodiments

As previously discussed, the disclosure only describes an *in vitro* HIV-1 CA assembly system. The CA protein from HIV-1 was purified in a soluble form. Immature particle formation was induced by adjusting the salt concentration (e.g., NaCl) to 1.8-2.4 M. The inventor reported that the efficiency of the reaction varied depending upon the capsid protein and salt concentrations. The disclosure does not provide any other working embodiments involving other HIV-1 structural proteins. The disclosure does not provide any other working embodiments involving non-HIV-1 structural proteins. Therefore, this single working embodiment is insufficient to support the full claim breadth.

Excessive Experimentation Required

Considering the vast structural and functional differences between various viral structural proteins, and the failure of the disclosure to provide adequate guidance pertaining to suitable purification schemes and in vitro assembly reaction conditions, it is clear that excessive experimentation would be required to practice the claimed invention.

Therefore, when all the aforementioned factors are considered *in*

toto, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-4 and 9-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gross *et al.* (1997) in view of Trono *et al.* (1989). As previously set forth, Gross and colleagues provide an *in vitro* Gag assembly system employing purified/solublized CA or purified/solublized CA/NC/nucleic acid. Various experimental parameters are disclosed (e.g., salt concentration, pH, protein concentration). Immature virion assembly is induced by diluting the purified protein(s) in a salt solution. See Table 1 (p. 596) for a description of suitable reaction conditions. The authors noted that particle formation occurs rapidly after the dialysis process begins. This teaching meets the following claim limitations: (i) maintenance of a viral structural protein in soluble form; (ii) initiation of virion capsid assembly by diluting the soluble structural protein in a salt solution; and (iv) monitoring immature virion assembly. This teaching does not

disclose utilizing this system to screen for putative antiviral agents or other modulators of the viral assembly process.

Trono *et al.* (1989) reported that HIV-1 site-directed Gag mutants were capable of inhibiting virion particle formation in cells in which they were cotransfected with wildtype proviral DNA. The authors conclude that such molecules may prove useful in the design of suitable HIV-1 therapeutics.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to test putative antivirals and regulators of assembly, as described by Trono *et al.* (1989), in the assembly system of Gross *et al.* (1997), since this would provide a facile method for identifying useful inhibitors or modulators of virion assembly.

Claims 7 and 8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gross *et al.* (1997) in view of Trono *et al.* (1989), and further in view of Vlasuk *et al.* (1989). Vlasuk and colleagues disclose the purification and storage of a soluble form of the HIV-1 $pr55^{gag}$ in GdnHCl solutions (2-6 M). It was noted (see MATERIALS AND METHODS, *Preparation of Guanidine-solublized p55*, p. 12107) the protein could be stored for several months under these conditions without appreciable loss of $pr55^{gag}$. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the full-length Gag precursor provided by Vlasuk *et al.* (1989) in the antiviral assay suggested by Gross *et al.* (1997) and Trono *et al.* (1989). Since Gross and colleagues teach that immature capsid assembly is initiated by dilution of the concentrated soluble protein by dialysis against salt, one of ordinary skill in the art would have reasonably expected the GdnHCl-purified Gag protein to assemble into immature virions when the proper salt concentratin was obtained.

Applicant is reminded that many of the arguments set forth in the last response were not directed toward specific claim limitations. As set forth above, the claims only require a soluble viral structural protein, means of triggering immature virion/capsid assembly, the addition of a putative antiviral agent, and a means for monitoring the reaction. In drafting acceptable claim language, applicant is directed toward the working embodiment set forth in the disclosure (i.e., An *in vitro* HIV-1 capsid assembly system employing the HIV-1 CA protein solublized in 6 M GdnHCl wherein capsid assembly is induced by dialyzing the concentrated soluble protein against a specific solution (1.8-2.4 M NaCl)). Appropriate amendment of the claim language to reflect the precise conditions described in the disclosure would be acceptable.

Correspondence

Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, Laurie Scheiner or James Housel, can be reached at (703) 308-1122 or (703) 308-4027, respectively. Any

inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose

telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

24 June, 2004